PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A19011PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/11604	International filing date *(day/month/year)* 20.10.2003	Priority date *(day/month/year)* 18.10.2002
International Patent Classification (IPC) or both national classification and IPC C12N15/12		
Applicant ATUGEN AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 16 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.04.2004	23.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Piret, B Telephone No. +31 70 340-1966

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11604

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-50 as originally filed

Claims, Numbers

1-26 received on 28.10.2004 with letter of 28.10.2004

Drawings, Sheets

1/11-11/11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 6, 8, 21-22 (industrial applicability)

   because:

   ☒ the said international application, or the said claims Nos. 6, 8, 21-22 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	none
	No:	Claims	1-26
Inventive step (IS)	Yes:	Claims	none
	No:	Claims	1-26
Industrial applicability (IA)	Yes:	Claims	1-5,7,9-20,23-26
	No:	Claims	6, 8, 21, 22: opinion reserved

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

In claim 6, the term "use of a nucleic acid [...] for the treatment and/or prevention of a disease [or] for wound healing" implies that claim 6 is directed at least in part to therapeutic methods applied to the human or animal body. The same applies to dependent claims 8 and 21-22. This subject-matter is considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. For the assessment of the present claims 6, 8 and 21-22 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 02/46465 A (KINGSMAN SUSAN MARY ;WARD NEIL RAYMOND (GB); KRIGE DAVID (GB); WHI) 13 June 2002 (2002-06-13)

D2: WO 00/77022 A (HUMAN GENOME SCIENCES, INC.) 21 December 2000 (2000-12-21)

D3: SHOSHANI TZIPORA ET AL: "Identification of a novel hypoxia-inducible factor 1-responsive gene, RTP801, involved in apoptosis." MOLECULAR AND CELLULAR BIOLOGY. UNITED STATES APR 2002, vol. 22, no. 7, April 2002 (2002-04), pages 2283-2293, XP002267737 ISSN: 0270-7306

1. Support (Article 6 PCT) and disclosure (Article 5 PCT)

1.1. The subject-matter of claims 1 relates in part to the use of PRF1 as a "downstream [drug] target" (claim 1), i.e. it has to be interpreted as relating to the use of agents (drugs) that affect the activity or expression of said factor. This includes not only testing (screening) methods, but also methods aimed at modulating the expression or activity of PRF1, which requires the disclosure of agents able to modulate said expression or activity. The disclosure of such

agents is limited to ribozymes, antisense oligonucleotides and siRNA that can hybridize with the polynucleotides having SEQ ID N°:2 and to antibodies directed against a polypeptide having SEQ ID N°:1, but claim 1 is not limited to the use of these agents. The nature (structure) of the other agents suitable for the use according to claim 1 is not disclosed sufficiently to enable a person skilled in the art to practice the methods of claim 1 over the whole scope of the claim. Therefore claim 1 does not meet the requirements of Article 5 PCT. The same objection applies to dependent claims 8, 14-17 and 21-26 which are also directed to the use of agents that interact with the factor or the nucleic acid "of any of the preceding claims". For instance, claim 17 is directed to the use of a nucleic acid that interacts with the PRF1 polypeptide (or a "part or derivative thereof"), but said nucleic acid is not disclosed in the application. The disclosure of a screening method suitable for testing whether some compounds have a desired effect is not a sufficient disclosure of the compounds having said effect. Consequently, the subject-matter of claims 1, 8, 14-17 and 21-26 will be examined with regards to novelty and inventive step only as far as it relates to the use of ribozymes, antisense oligo- or polynucleotides and siRNA that can hybridize with the gene encoding PRF1 and to antibodies directed against the PRF1 polypeptide.

1.2. The description and Figure 1 convey the impression that the pathway in which the claimed factor (PRF1) participates is only one of many distinct pathways of which PI3-K is an upstream effector. However, the only downstream effect of PRF1 that is documented in the application or in the prior art is an effect on cancer cell motility, growth and survival (apoptosis). Nothing in the file or in the prior art suggests that PRF1 could participate in other PI3-K-, Akt- or HIF1alpha-mediated pathways such as those involved in regulation of glucose metabolism, response to amino-acid or glucose deprivation, diabetes, wound healing, stress response other than hypoxia/oxidative stress response, or any other "PI 3-kinase pathway regulated process". Similarly, it is not apparent either how the claimed PRF1 factor is technically linked to some of the listed "conditions involving the PI3-kinase pathway" such as mucocutaneous lesions, "trichilemmon-mas", macrocephaly or mental retardation, or involved in modulating or "diagnosing" wound healing. Therefore the possibility to put to practice some of the uses of claims 2 and 4-26 appears to be purely speculative. These claims do not meet the requirements of Article 6 PCT (according to which the claims must be fully supported by the description) over their whole scope and their subject-matter is not sufficiently disclosed to enable a person skilled in the art to put the invention to practice over the whole scope of the claims without undue experimentation (Article

5 PCT). For this reason, the subject-matter of the claims will be examined with regards to novelty and inventive step only as far as it relates to the effects of PRF1 on response to hypoxia/oxidative stress, apoptosis, cancer, metastasis, tumorigenesis, cell migration, cell motility and cell growth in extracellular matrix.

2. Clarity (Article 6 PCT)

The following terms are vague regarding the technical features to which they refer and can have different meanings for the person skilled in the art, depending on the context, thereby rendering the claims unclear (Article 6 PCT) and preventing from distinguishing the claimed subject-matter from the prior art:

- "essentially complementary" in claims 1, 2, 4-7, 9-12, 20 and 23
- "a fragment or a derivative thereof" in claims 1 and 4-7, "part or derivative thereof" in claims 9-12, 14, 16-18, 20 and 23 and "part thereof" in claims 1, 2, 4-7, 9-12, 20 and 23; a "fragment" or "part" of a protein can be as small as one amino-acid; a "fragment" or "part" of a polynucleotide can be as small as a single nucleotide; a "derivative" of a polypeptide can be any other polypeptide.
- "PI 3-kinase pathway" in claim 1, whereas there seem to be several pathways in which PI3-K participates, and whereas PRF1 seems to be involved in only one of these
- "PI 3-kinase pathway regulated process" in claims 2 and 21
- "stress response" in claims 2 and 22 whereas a very large number of conditions can be considered as a "stress"
- "the cells being involved in said disease", "hyperactivation of the PI 3-kinase pathway" and "increased aggressive behaviour" in claim 8
- "any pathological conditions involving the PI 3-kinase pathway" in claims 9-12 and 23 where said conditions are not further characterized
- "functional nucleic acids" and "natural compounds" in claim 25 and "small molecules" in claims 13 and 25

3. Novelty and inventive step (Article 33 PCT)

3.1. D1 and D2 disclose a nucleic acid having a sequence identical to SEQ ID N°:2 of the present application, encoding a polypeptide having a sequence identical to SEQ ID N°:1, and also disclose their use as markers of cancer cells

(D1, Sequences 25-26, Example 5; D2, sequence SEQ ID N°:85, p.219 and on) and as targets of anticancer therapy. D3 discloses the expression of PRF1 in response to hypoxia and reminds (p.2291, discussion, 1st paragraph) that genes induced by hypoxia may play a role in several processes including wound healing, stroke, retinopathy and carcinogenesis. D1 also suggests that such hypoxia-responsive genes may be important targets for the development of drugs modulating these pathological conditions. Therefore, the subject-matter of claims 1-26, i.e. the use of PRF1 as a marker of pathological processes or as a target for investigating or treating such pathologies, or for developing or manufacturing drugs to be used against said pathologies, does not meet the requirements of Article 33 PCT (novelty and inventive step).

3.2. The subject-matter of the application relates in part to the use of PRF1 as a marker of the activity of the PI3-kinase *in vitro*. Since the role of PI3-K in the expression/activity of PRF1 was not disclosed or suggested in the prior art, the specific use of PRF1 as a marker of PI3-K activity might form the basis of a claim that would meet the requirements of Article 33 PCT, provided that the objections V.1 and V.2 (clarity and support) of above are overcome.

3.3. In addition, the description discloses (Examples 9 and 10) the inhibition of PRF1 expression/activity by the use of antisense nucleic acids or interfering RNA. The technical effect of this inhibition is an inhibition of tumour cell proliferation/motility in matrigel (Example 9) and of tumour growth (Example 10) in some particular cell types. This technical effect was not disclosed or suggested in the prior art. Therefore, the subject-matter relating specifically to the means and methods of inhibiting PRF1 for treating some types of cancer, insofar as said means and methods are clearly defined and supported by the description (see V.1 and V.2 above), might form the basis of claims that would meet the requirements of Article 33 PCT.

PCT/EP 03/11604
atugen AG
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New Claims

1. In vitro use of a polypeptide factor, whereby the factor

a) comprises an amino acid sequence according to SEQ ID NO. 1;

b) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

c) is encoded by a nucleic acid, whereby the

ca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

cb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

cc) the nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

or a fragment or a derivative thereof as a downstream target or a downstream marker of the PI 3-kinase pathway, preferably as a downstream drug target of the PI 3-kinase pathway.

2. In vitro use of a polypeptide factor, whereby the factor

a) comprises an amino acid sequence according to SEQ ID NO. 1;

b) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

c) is encoded by a nucleic acid, whereby the

ca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

cb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

cc) the nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

as a marker for a process, whereby the process is a PI 3-kinase pathway regulated process, preferably a process selected from the group comprising glucose metabolism, amino acid and glucose deprivation processes, diabetes, wound healing, stress response, apoptosis, metastasis, tumorigenesis, cell migration, cell motility in extracellular matrix and cell growth in extracellular matrix.

3. Use according to claim 2, whereby the factor is a marker for transformed cells, preferably for invasive cells.

4. Use of a polypeptide factor, whereby the factor

a) comprises an amino acid sequence according to SEQ ID NO. 1;

b) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

c) is encoded by a nucleic acid, whereby the

ca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

cb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

cc) the nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

or a fragment or derivative thereof for the manufacture of a medicament for the treatment and/or prevention of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies,

or whereby the medicament is for wound healing.

5. Use of a polypeptide factor, whereby the factor

a) comprises an amino acid sequence according to SEQ ID NO. 1;

b) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

c) is encoded by a nucleic acid, whereby the

ca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

cb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

cc) the nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

or a fragment or derivative thereof for the manufacture of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies,

or whereby the diagnostic agent is for wound healing.

6. Use of a nucleic acid, whereby such nucleic acid is

a) a nucleic acid coding for a factor, whereby the factor is
   i) a polypeptide comprising an amino acid according to SEQ ID NO. 1; or
   ii) a polypeptide having a sequence according to data bank entries gi 9506687 or NP_061931;
b) a nucleic acid coding for a factor, whereby the nucleic acid comprises
   i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

c) a nucleic acid coding for a factor, whereby the nucleic acid would hybridise, for the degeneracy of the genetic code, to a nucleic acid according to b), or a part thereof; or

d) a nucleic acid coding for a factor, whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to b) or a part thereof;

or a fragment or a derivative thereof for the treatment and/or prevention of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies.

or whereby the medicament is for wound healing.

7. Use of a nucleic acid, whereby such nucleic acid is

a) a nucleic acid coding for a factor, whereby the factor is
   i) a polypeptide comprising an amino acid according to SEQ ID NO. 1; or
   ii) a polypeptide having a sequence according to data bank entries gi 9506687 or NP_061931;

b) a nucleic acid coding for a factor, whereby the nucleic acid comprises
   i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

c) a nucleic acid coding for a factor, whereby the nucleic acid would hybridise, for the degeneracy of the genetic code, to a nucleic acid according to b), or a part thereof; or

d) a nucleic acid coding for a factor, whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to b) or a part thereof;

or a fragment or derivative thereof for the manufacture of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies

or whereby the diagnostic agent is for wound healing.

8. Use according to any of claims 1 and 3 to 7, whereby

the disease is characterized in that the cells being involved in said disease lack PTEN activity, or show a hyperactivation of the PI 3-kinase pathway, or show an increased aggressive behaviour, or are tumor cell, preferably cells of a late stage tumor.

9. In vitro use of a polypeptide factor, whereby the factor

a) comprises an amino acid sequence according to SEQ ID NO. 1;

b) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

c) is encoded by a nucleic acid, whereby the

ca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

cb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

cc) the nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

or a part or a derivative thereof as a target molecule for the development of a medicament for the treatment and/or prevention of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

or whereby the medicament is for wound healing.

10. In vitro use of a polypeptide factor, whereby the factor

a) comprises an amino acid sequence according to SEQ ID NO. 1;

b) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

c) is encoded by a nucleic acid, whereby the

ca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

cb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

cc) the nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

or a part or a derivative thereof as a target molecule for the development of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

or whereby the diagnostic agent is for wound healing.

11. In vitro use of a nucleic acid, whereby said nucleic acid is

a) a nucleic acid coding for a factor, whereby the factor is
   i) a polypeptide comprising an amino acid according to SEQ ID NO. 1; or
   ii) a polypeptide having a sequence according to data bank entries gi 9506687 or NP_061931;

b) a nucleic acid coding for a factor, whereby the nucleic acid comprises
   i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or
   ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

c) a nucleic acid coding for a factor, whereby the nucleic acid would hybridise, for the degeneracy of the genetic code, to a nucleic acid according to b), or a part thereof; or

d) a nucleic acid coding for a factor, whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to b) or a part thereof;

or a part or a derivative thereof as a target molecule for the development of a medicament for the treatment and/or prevention of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

or whereby the medicament is for wound healing.

12. In vitro use of a nucleic acid, whereby said nucleic acid is

a) a nucleic acid coding for a factor, whereby the factor is
   i) a polypeptide comprising an amino acid according to SEQ ID NO. 1; or
   ii) a polypeptide having a sequence according to data bank entries gi 9506687 or NP_061931;

b) a nucleic acid coding for a factor, whereby the nucleic acid comprises
   i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or
   ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

c) a nucleic acid coding for a factor, whereby the nucleic acid would hybridise, for the degeneracy of the genetic code, to a nucleic acid according to b), or a part thereof; or

d) a nucleic acid coding for a factor, whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to b) or a part thereof;

or a part or a derivative thereof as a target molecule for the development of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

or whereby the diagnostic agent is for wound healing.

13. The use according to any of claims 9 to 12, characterised in that the medicament and/or the diagnostic agent comprises an agent, which is selected from the group comprising antibodies, peptides, anticalines, small molecules, antisense molecules, aptameres, spiegelmers and RNAi molecules.

14. The use according to claim 13, characterised in that the agent interacts with the factor according to any of the preceding claims or a part or derivative thereof.

15. The use according to claim 13, characterised in that the agent interacts with the nucleic acid as defined in any of the preceding claims, in particular with mRNA, genomic nucleic acid or cDNA for the polypeptide factor as defined in any of the preceding claims.

16. Use of a polypeptide which interacts with the polypeptide factor, or a part or derivative thereof, for the development or manufacture of a medicament for the treatment and/or prevention of a disease and/or for the manufacture of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway, whereby such conditions are selected from the group comprising

endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies

or whereby the medicament and/or the diagnostic agent is for wound healing,

whereby the polypeptide is selected from the group, which comprises antibodies against the polypeptide factor or a part or derivative thereof, and polypeptides binding the polypeptide factor or a part or derivative thereof.

17. Use of a nucleic acid which interacts with the polypeptide factor or a part or derivative thereof, for the development or manufacture of a medicament for the treatment and/or prevention of a disease and/or for the manufacture of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies

or whereby the medicament and/or the diagnostic agent is for wound healing,

whereby the nucleic acid is selected from the group which comprises aptamers and spiegelmers.

18. Use of a nucleic acid which interacts with a nucleic acid coding for the polypeptide factor as defined in any of the preceding claims or a part or derivative thereof, for the development or manufacture of a medicament for the treatment and/or prevention of a disease and/or for the manufacture of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies

or whereby the medicament and/or the diagnostic agent is for wound healing,

whereby the interacting nucleic acid is an antisense oligonucleotide, a ribozyme and/or siRNA.

19. The use according to claim 18, characterised in that the nucleic acid coding for the polypeptide factor or a part or derivative thereof is the cDNA, mRNA or hnRNA.

20. Use of a kit for the characterisation of a disease or a condition which is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

whereby such conditions are selected from the group comprising endometrial cancer, colorectal carcinomas, gliomas, endometrial cancers, adenocarcinomas, endometrial hyperplasias, Cowden's syndrome, hereditary non-polyposis colorectal carcinoma, Li-Fraumene's syndrome, breast-ovarian cancer, prostate cancer, Bannayan-Zonana syndrome, LDD (Lhermitte-Duklos' syndrome) hamartoma-macrocephaly diseases including Cow disease (CD) and Bannayan-Ruvalcaba-Rily syndrome (BRR), mucocutaneous lesions, such as trichilemmonmas, macrocephaly, mental retardation, gastrointestinal harmatomas, lipomas, thyroid adenomas, fibrocystic disease of the

breast, cerebellar dysplastic gangliocytoma and breast and thyroid malignancies, and wound healing,

whereby the kit comprises at least one agent which is selected from the group comprising the polypeptide factor as defined in any of the preceding claims or a part or derivative thereof, antibodies specific for said polypeptide factor or a part or derivative thereof, polypeptides interacting with said polypeptide factor or a part or derivative thereof, polypeptides interacting with

a) a nucleic acid coding for a factor, whereby the factor is
   i) a polypeptide comprising an amino acid according to SEQ ID NO. 1; or
   ii) a polypeptide having a sequence according to data bank entries gi 9506687 or NP_061931;
b) a nucleic acid coding for a factor, whereby the nucleic acid comprises
   i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or
   ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;
c) a nucleic acid coding for a factor, whereby the nucleic acid would hybridise for the degeneracy of the genetic code, to a nucleic acid according to b) or a part thereof; or
d) a nucleic acid coding for a factor, whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to b) or a part thereof;

nucleic acids interacting with said polypeptide factor or a part or derivative thereof, and nucleic acids interacting with

a) a nucleic acid coding for a factor, whereby the factor is
   i) a polypeptide comprising an amino acid according to SEQ ID NO. 1; or
   ii) a polypeptide having a sequence according to data bank entries gi 9506687 or NP_061931;
b) a nucleic acid coding for a factor, whereby the nucleic acid comprises
   i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

c) a nucleic acid coding for a factor, whereby the nucleic acid would hybridise for the degeneracy of the genetic code, to a nucleic acid according to b) or a part thereof; or

d) a nucleic acid coding for a factor, whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to b) or a part thereof;

and optionally at least one other compound.

21. Use according to any of claims 1 to 20, whereby the polypeptide factor is involved in a biological process, whereby the process is a PI 3-kinase pathway regulated process.

22. The use according to claim 21, whereby the process is

a process selected from the group comprising glucose metabolism, amino acid and glucose deprivation processes, diabetes, wound healing, stress response, apoptosis, metastasis, tumorigenesis, cell migration, cell motility in extracellular matrix and cell growth in extracellular matrix.

23. A method for the screening of an agent for the manufacture of a medicament for the treatment and/or prevention of a disease and/or for the manufacture of a diagnostic agent for the diagnosis of a disease,

whereby the disease is selected from the group comprising late stage tumor, metastatic cancer, diabetes and any pathological conditions involving the PI 3-kinase pathway,

or whereby the medicament and/or the diagnostic agent is for wound healing,

comprising the following steps:

a) providing a candidate compound,

b) providing an expression system for a polypeptide factor , whereby the factor

ba) comprises an amino acid sequence according to SEQ ID NO. 1;

bb) has an amino acid sequence according to data bank entries gi 9506687 or NP_061931;

bc) is encoded by a nucleic acid, whereby the

bca) nucleic acid comprises

i) a nucleic acid according to SEQ ID NO. 2 or SEQ ID NO. 3; or

ii) a nucleic acid sequence according to data bank entries gi 9506686 or NM_019058;

bcb) the nucleic acid codes for said factor and whereby the nucleic acid would hybridise but for the degeneracy of the genetic code, to a nucleic acid according to ca) or a part thereof; or

bcc) a nucleic acid codes for said factor and whereby the nucleic acid hybridises under stringent conditions to a nucleic acid which is essentially complementary to the nucleic acid according to ca) or a part thereof;

and/or a system, preferably an activity system, detecting the activity of said polypeptide factor;

c) contacting of the candidate compound with the expression system for said polypeptide factor and/or the system, preferably an activity system, detecting activity of said polypeptide factor;

d) determining if the expression and/or the activity of said polypeptide factor is changed under the influence of the candidate compound.

24. Method according to claim 23, characterised in that the candidate compound is contained in a library of compounds.

25. The method according to claim 23 or 24, characterised in that the candidate compound is selected from the group of classes of compounds comprising peptides, proteins,

antibodies, anticalines, functional nucleic acids, natural compounds and small molecules.

26. The method according to claim 25, characterised in that the functional nucleic acids are selected from the group which comprises aptameres, aptazymes, ribozymes, spiegelmers, antisense oligonucleotides and siRNA.